OBSERVATION

Morphologic Changes of Acquired Melanocytic Nevi With Eccentric Foci of Hyperpigmentation ("Bolognia Sign") Assessed by Dermoscopy

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Background: Melanocytic nevi with eccentric foci of hyperpigmentation ("Bolognia sign") can be considered as a melanoma-simulating type of acquired melanocytic nevus. We report on the morphologic changes of this type of melanocytic nevus over a 39-month period of dermoscopic follow-up.

Observations: A 5-year-old girl had a 4-mm brown papule with a peripheral blue-black area on her right upper arm. The eccentric focus of the hyperpigmentation corresponded dermoscopically to a blue-gray area of pigmentation associated with irregular brown-black globules or dots and partially with a superficial black network. After 39 months, a globular type of acquired melanocytic nevus was detectable, which clinically and dermoscopically appeared to be completely benign. A nearly identical situation was observed in 5 other melanocytic nevi, underlining the involution of the pigmented foci in these nevi. The histopathologic diagnoses of 2 lesions were consistent with a compound type of acquired melanocytic nevus with eccentric foci of hyperpigmentation.

Conclusions: Dermoscopy allows identification of a morphologic pathway of modifications, probably typical for this type of melanocytic nevus in children, and therefore enables avoidance of surgical excision with attendant hypertrophic scarring in children. Conversely, in adults, when dermoscopic follow-up of melanocytic nevi reveals eccentric foci of hyperpigmentation, surgical excision of the lesion is indicated.

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MELANOCYTIC NEVI WITH eccentric foci of hyperpigmentation, described in 1994 by Bolognia et al[1] as "small dark dots," can be considered as a melanoma-simulating type of acquired melanocytic nevus. The rationale for this assumption is that eccentric peripheral hyperpigmentation has also often been found in melanoma.[2] Clinically, eccentric small dark dots appear as roundish areas of brown to black hyperpigmentation 3 mm or smaller localized peripherally; a few also have a slightly blue-gray hue.[1] Histopathologically, the eccentric focal hyperpigmentation is due in most cases (nearly 70% of the cases in the original series of Bolognia et al[1]) to an increase in the melanin content of the epidermal melanocytes and/or keratinocytes, which usually involves an increased number of superficial dermal melanophages. Another cause for the small dark dots is the increase of melanophages and/or increase of melanin in melanocytes in the papillary dermis and the upper reticular dermis. About 3% of the small dark dots represent a focus of melanoma within a preexisting nevus.[1] Considering that eccentric foci of hyperpigmentation can also be found in combined nevi, Clark nevi,[3,4] and in other types of nevi, we suggest that the name "Bolognia sign"can be given to eccentric foci of hyperpigmentation within nevi.

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Herein, we report a case of a 5-year-old girl with several melanocytic nevi with eccentric foci of hyperpigmentation and emphasize the morphologic changes detected during 39 months of dermoscopic follow-up.

REPORT OF A CASE

In June 2001, a 5-year-old girl was brought by her mother to the National Cancer Institute of Aviano, Italy, presenting with a pigmented lesion on the right upper arm. The 4-mm lesion consisted of a brown papule with a blue-black area situated peripherally.The child had another similar lesion on the back. Because of their appearance, the lesions were clinically diagnosed as melanocytic nevi with eccentric foci of hyper-

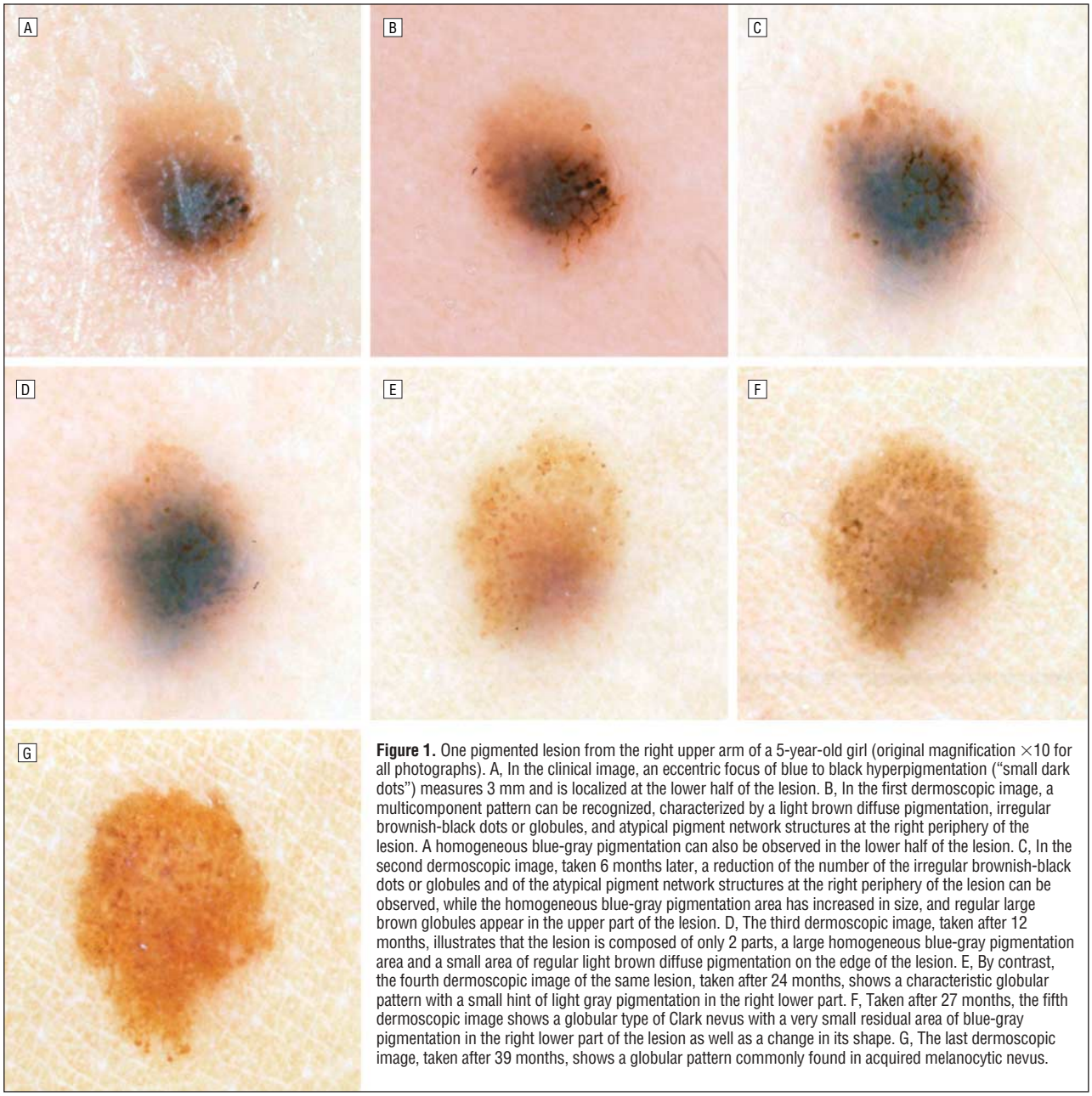

Figure 1. One pigmented lesion from the right upper arm of a 5-year-old girl (original magnification ×10 for all photographs). A, In the clinical image, an eccentric focus of blue to black hyperpigmentation ("small dark dots") measures 3 mm and is localized at the lower half of the lesion. B, In the first dermoscopic image, a multicomponent pattern can be recognized, characterized by a light brown diffuse pigmentation, irregular brownish-black dots or globules, and atypical pigment network structures at the right periphery of the lesion. A homogeneous blue-gray pigmentation can also be observed in the lower half of the lesion. C, In the second dermoscopic image, taken 6 months later, a reduction of the number of the irregular brownish-black dots or globules and of the atypical pigment network structures at the right periphery of the lesion can be observed, while the homogeneous blue-gray pigmentation area has increased in size, and regular large brown globules appear in the upper part of the lesion. D, The third dermoscopic image, taken after 12 months, illustrates that the lesion is composed of only 2 parts, a large homogeneous blue-gray pigmentation area and a small area of regular light brown diffuse pigmentation on the edge of the lesion. E, By contrast, the fourth dermoscopic image of the same lesion, taken after 24 months, shows a characteristic globular pattern with a small hint of light gray pigmentation in the right lower part. F, Taken after 27 months, the fifth dermoscopic image shows a globular type of Clark nevus with a very small residual area of blue-gray pigmentation in the right lower part of the lesion as well as a change in its shape. G, The last dermoscopic image, taken after 39 months, shows a globular pattern commonly found in acquired melanocytic nevus.

pigmentation. During the follow-up examinations, which were performed every 6 months for a period of 39 months, both lesions showed evident changes. Moreover, at least 6 new similar lesions appeared on the back, trunk, and arms. During each of the follow-up visits, all of the lesions were evaluated using standard dermoscopic criteria and were photographed with Dermaphot equipment (Heine, Herrsching, Germany), producing dermoscopic images at a fixed magnification of ×10. Herein, we describe 3 of these lesions: those situated on the right upper arm, the trunk, and the left thigh.

Clinically, the right upper arm lesion (**Figure 1**A) showed an eccentric focus of blue to black hyperpigmentation on its lower half. In the first dermoscopic image of this lesion (Figure 1B), a multicomponent pattern can be recognized, characterized by a light brown diffuse pigmentation with regular brown globules or dots in the upper part of the lesion, irregular brownish-black globules or dots, and a superficial black network on the right periphery of the lesion. A homogeneous blue-gray pigmentation can also be observed in the lower half of the lesion. In the second dermoscopic image (Figure 1C), taken 6 months later, a reduction can be seen in the superficial black network and the number of irregular brownish-black globules or dots on the right periphery of the lesion, while regular larger brown globules appear in the upper part of the lesion, and the homogeneous blue-gray pigmented area in the lower half of the lesion has increased in size.

The third dermoscopic image of the same lesion (Figure 1D), taken 12 months after the first examination, shows a lesion composed of a homogeneous blue-gray pigmentation and a small area of regular, light brown, dif-

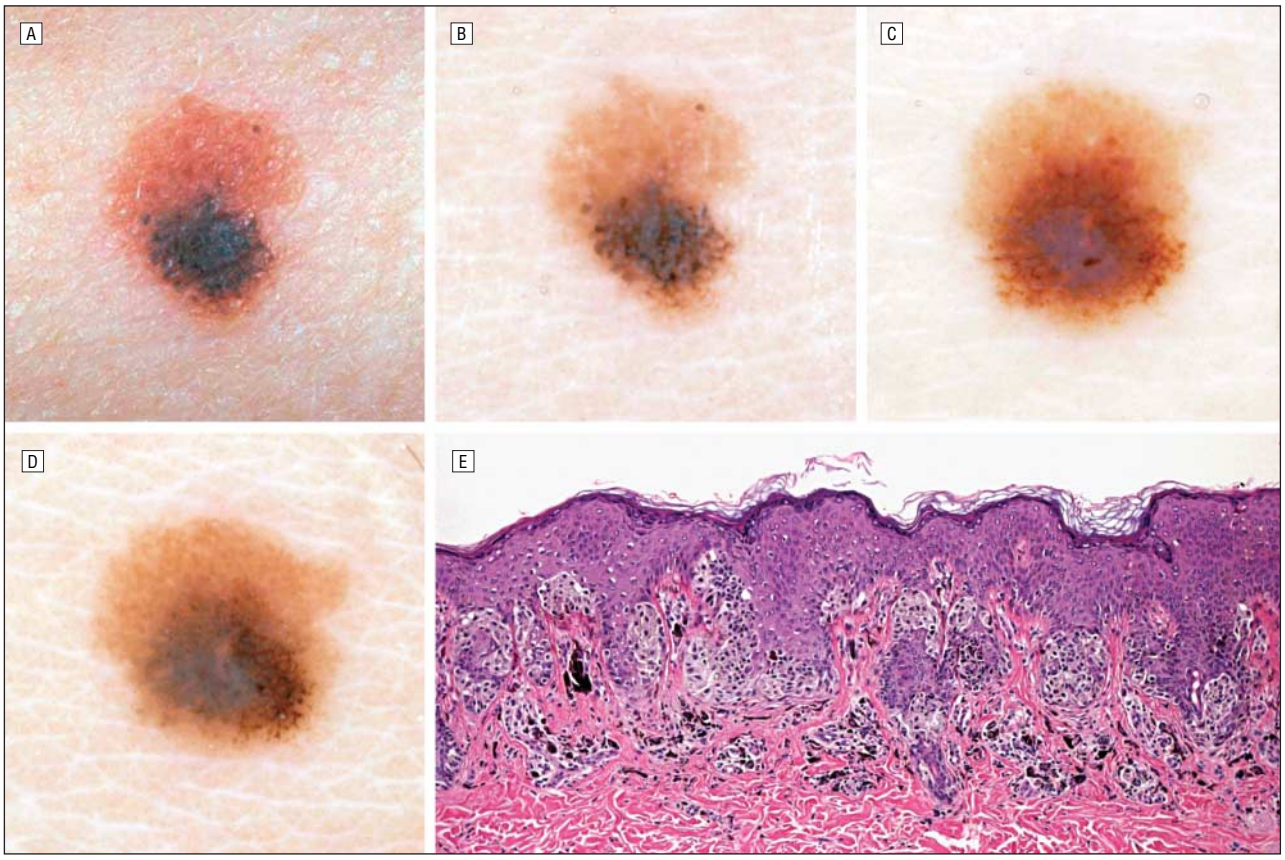

Figure 2. One pigmented lesion from the trunk of a 5-year-old girl (original magnification ×10 for panels A-D; ×100 for panel E). A, The clinical image shows an eccentric focus of blue to black hyperpigmentation ("small dark dots") measuring 3 mm and localized in the lower half of the lesion. B, The first dermoscopic image shows a multicomponent pattern characterized by a homogeneous light brown pigmentation, irregular brown-black globules and dots, and an area of blue-gray pigmentation. C, The second dermoscopic image, taken 6 months later, shows a reduction in the number of irregular brown-black globules and dots and an increase of the blue-gray pigmentation. D, The third dermoscopic image, taken 9 months from the baseline evaluation, shows an increase in the number of atypical pigment network structures and a progressive increase in the blue-gray pigmentation. E, Histopathologic analysis reveals a compound dysplastic nevus with focal hyperpigmentation, nests of melanocytes in the epidermis and papillary dermis, and melanophages in the papillary dermis.

fuse pigmentation and brown globules or dots on the edge of the lesion. By contrast, a characteristic globular pattern was clearly recognizable in the fourth dermoscopic image (Figure 1E), taken at the 24-month follow-up. This pattern was typified by regular brown globules and dots extending throughout the entire lesion with a small light hint of blue-gray pigmentation in the right lower part. In the fifth dermoscopic image of the same lesion (Figure 1F), taken 27 months from the baseline visit, a globular type of melanocytic nevus with a very small area of residual blue-gray pigmentation in the right lower part is present. In addition, a slight change in its shape is now identifiable. The last dermoscopic image of the same lesion (Figure 1G), taken at 39 months, shows a globular pattern commonly found in acquired melanocytic nevus. Owing to its completely benign appearance, this lesion was not excised.

In January 2003, 19 months after the baseline evaluation, a new asymmetrical lesion appeared on the patient's trunk. Clinically, this lesion (**Figure 2**A) showed an eccentric focus of blue to black hyperpigmentation in its lower half. Dermoscopically, this image (Figure 2B) was composed of a homogeneous light brown pigmentation in the upper part and irregular brown-black globules and dots in the lower part. In addition, an area of blue-gray pigmentation was also observed in the lower half of the lesion. After 6 months (Figure 2C), a reduction was noted in the number of irregular brown-black globules and dots along with an increase in the area of blue-gray pigmentation and of the superficial black network. After nine months, the blue area had increased progressively, while the superficial black network structures had become more evident. Therefore, in September 2003, after a total follow-up of 9 months, the lesion was excised, and histopathologic analysis revealed a compound type of acquired melanocytic nevus with a focal increase of melanophages in the papillary dermis (Figure 2E).

In May 2004, another new lesion appeared on the patient's left thigh. Clinically, the lesion (**Figure 3**A) showed an eccentric focus of blue to black hyperpigmentation that measured 3 mm and was localized on the right side of the lesion. Dermoscopically, the lesion (Figure 3B) was characterized by a homogeneous light brown pigmentation with regular brown globules and irregular dark dots localized on the right periphery. In this area, a blue-gray pigmentation was also observed. In October 2004, after 5 months of follow-up, the lesion showed subtle changes (Figure 3C), with a slight reduction of the blue area and of the irregular brown dots and globules. The blue area was excised and a punch biopsy specimen taken to obtain a better histopathologic characterization of this area. Histopathologically, the

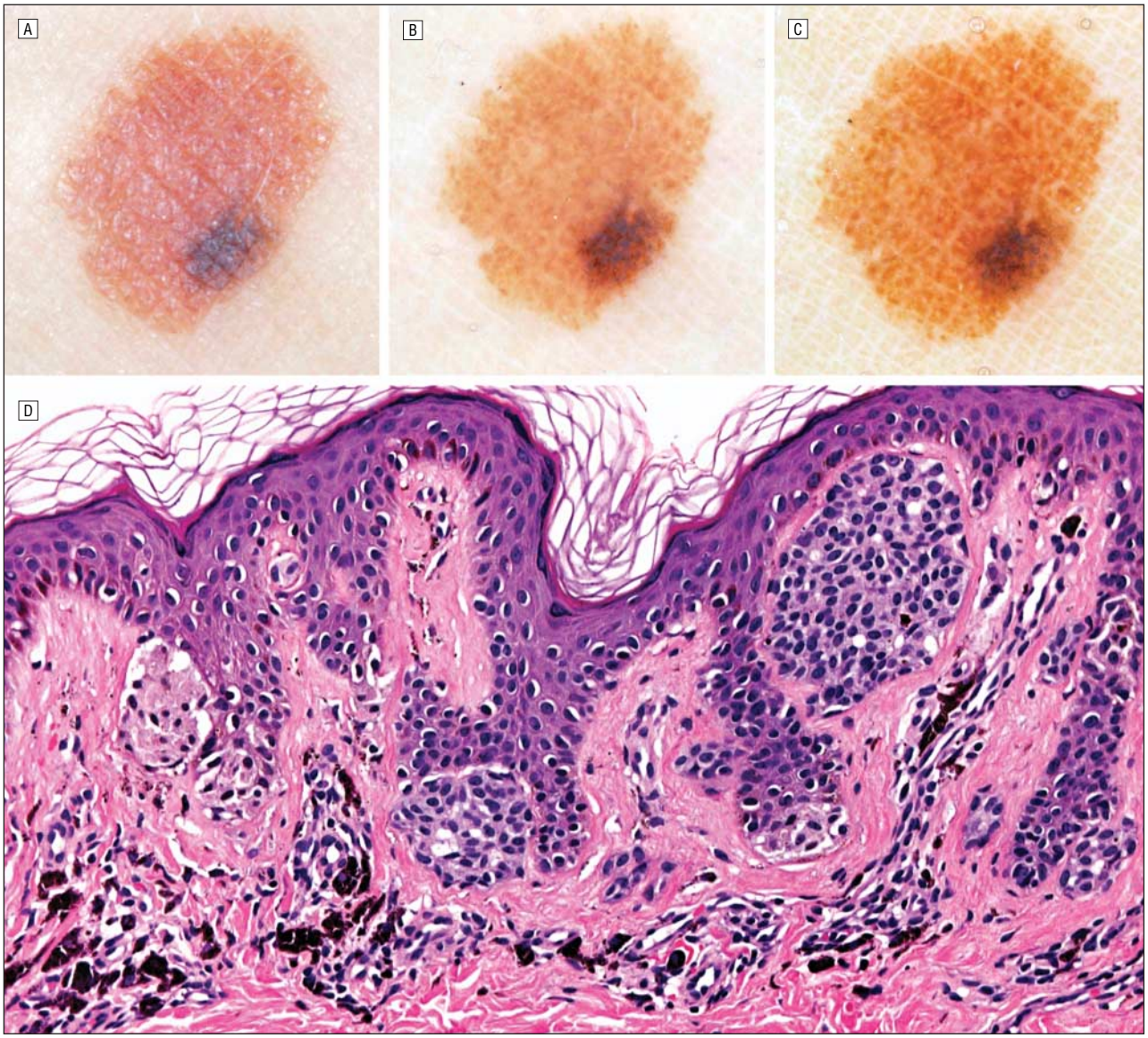

Figure 3. One pigmented lesion from the left thigh of a 5-year-old girl (original magnification ×10 for panels A-C; ×200 for panel D). A, The clinical image shows an eccentric focus of blue to black hyperpigmentation ("small dark dots") that measures 3 mm and is localized at the right periphery of the lesion. B, The first dermoscopic image shows homogeneous light brown pigmentation, regular light brown globules, and irregular dark dots localized at the right periphery of the lesion. In this area, blue-gray pigmentation can also be observed. C, The second dermoscopic image, taken 5 months later, shows a lesion with subtle changes: only a mild reduction of the blue-gray area and of the irregular dark dots. D, Histopathologic analysis reveals a compound dysplastic nevus with focal hyperpigmentation, nests of melanocytes in the epidermis and papillary dermis, and melanophages in the papillary dermis.

presence of nests of small regular melanocytes at the dermoepidermal junction and in the papillary dermis were observed intermingled with numerous melanophages in the papillary dermis corresponding to the blue-black hyperpigmentation. The histopathologic diagnosis was consistent with a compound type of acquired melanocytic nevus (Figure 3D). Clinically and dermoscopically, this nevus was similar to other melanocytic nevi with eccentric foci of hyperpigmentation present in this patient.

COMMENT

From the clinical point of view, acquired melanocytic nevi with eccentric foci of hyperpigmentation are simulators of melanoma arising in a preexisting nevus. In fact, in these nevi, clinical features such as asymmetry and color variegation are strongly suggestive of melanoma.[1] In addition, melanocytic nevi with eccentric foci of hyperpigmentation may also be confused with the eccentric peripheral hyperpigmented type of Clark nevus described by Hofmann-Wellenhof et al.[3] Clark nevi (atypical melanocytic nevi) are acquired melanocytic lesions named after Wallace H. Clark, whose research team first drew attention to this particular type of nevus by studying numerous melanocytic nevi in patients with concomitant melanomas.[5] For the clinical diagnosis of Clark nevus, at least 3 of the following characteristics must be present: diameter greater than 5 mm, ill-defined borders, irregular margin, varying color shades within the lesion, and the simultaneous presence of papular and macular components. Common melanocytic nevi

are those that show fewer than 3 of these features of atypia.[6,7] Eccentric peripheral hyperpigmented type of Clark nevi are dermoscopically characterized by a reticular or a reticular-homogeneous pattern with an area of eccentrically situated hyperpigmentation reaching the border of the lesion. In some instances, an eccentric peripheral hyperpigmented type of Clark nevus also has an atypical pigment network that looks like a melanoma.[3]

Other differential diagnoses of acquired melanocytic nevi with eccentric foci of hyperpigmentation include combined nevi.[8-10] The combined nevus originally referred to the occurrence of a common melanocytic nevus within a blue nevus.[8] The term *combined nevi* was coined in 1977 by Gartmann and Muller[9] to describe nevi characterized by the presence of 2 or more of the following types of nevi: common nevi, blue nevi, cellular blue nevi, and Spitz nevi. According to some authors, any kind of melanocytic nevus (common acquired nevus, congenital nevus, or a Clark nevus) may be combined with other melanocytic nevi or with a blue or a Spitz nevus.[10] The combination may be both of acquired lesions and of acquired plus congenital lesions. In fact, cases of a congenital nevus combined with a blue nevus, Spitz nevus, or Clark nevus as well as cases of common intradermal melanocytic nevus combined with a Clark nevus have been identified by some authors.[4] Combined nevi, in particular the variant combined Clark nevus, are difficult to interpret clinically and histopathologically and may be misdiagnosed as melanoma associated with a nevus.[4]

The eccentric foci of hyperpigmentation of the 3 nevi described herein correspond dermoscopically to blue-gray areas of pigmentation associated with irregular globules and dots and partially with a superficial black network.[11] During the development of the first lesion, the superficial black network and the irregular globules and dots progressively disappeared, while the blue-gray areas at first increased, reaching their full development after 1 year of follow-up. Later on, however, the blue-gray areas regressed completely and were replaced by regular slightly pigmented dots and globules throughout the nevus. After 39 months of follow-up, a globular type of acquired melanocytic nevus was detectable, which appeared completely benign both clinically and dermoscopically.

A nearly identical observation was made in 5 other melanocytic nevi in this child, underlining the involution of the pigmented foci in these nevi. Based on our observations in children, eccentric foci of hyperpigmentation within melanocytic nevi might be considered a particular phenotypic pathway in the early phase of development toward a globular type of acquired melanocytic nevus. In an earlier study on the dermoscopic follow-up of a pigmented Spitz nevus in a child during its growing phase, our research team was able to demonstrate its evolution from globular to starburst and finally to a homogeneous pattern.[12]

Therefore, we particularly underline the importance of dermoscopic follow-up in children for the management of melanocytic nevi with foci of eccentric hyperpigmentation. Using dermoscopic follow-up observation, we can identify a morphologic pathway of modifications, probably typical for this type of melanocytic nevus, and therefore avoid surgical excision. These findings are not applicable to similar lesions in adults because this type of atypical nevus should be considered as the most relevant simulator of early melanoma within Clark nevi.[3] In fact, eccentric peripheral hyperpigmentation has been found in 25.3% of melanomas and in only 4.5% of benign melanocytic lesions.[13] In adults, the eccentric foci of hyperpigmentation within nevi could be a sign of a possible morphologic transformation of an atypical nevus (Clark nevus) into a cutaneous melanoma,[14] so in our opinion, this type of nevus has to be excised. In children, dermoscopic follow-up of melanocytic nevi with eccentric foci of hyperpigmentation might represent a valid alternative to surgical excision.

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